Applicant: ROLFE C. ANDERSON et al.

Serial No: 09/751,657 Filed: December 31, 2000

## AMENDMENTS TO THE CLAIMS

Claims 1 – 40 (previously cancelled in Preliminary Amendment)

Claims 41 – 44 (presently cancelled)

45. (Presently Amended) A low-volume hybridization <u>device</u> <del>chamber</del>, comprising:

a base,

a reaction chamber disposed in said base, said reaction chamber being bound by a flexible diaphragm, and

a probe array disposed in said reaction chamber.

- 46. (Presently Amended) The low-volume hybridization <u>device</u> <del>chamber</del> of claim 45, wherein said reaction chamber has a volume in the range of 0.1 to 100 μl.
- 47. (Presently Amended) The low-volume hybridization <u>device</u> <del>chamber</del> of claim 45, wherein said reaction chamber has a volume in the range of 1 to 20 μl.
- 48. (Presently Amended) The low-volume hybridization <u>device</u> <del>chamber</del> of claim 45 [[1]], further comprising:

a pneumatic system for moving said flexible diaphragm.

49. (pending as filed) A hybridization device, comprising:

a base,

a fluidic chamber disposed in said base, said fluidic chamber having a hybridization array disposed therein,

a porous membrane disposed in said fluidic chamber opposite said array,

a pneumatic port disposed in said base, said pneumatic port addressing said porous membrane, and

a thermal control device for controlling the temperature in the array.

Claims 50 – 65 (previously cancelled in Preliminary Amendment)

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- 66. (New) The low-volume hybridization device of claim 45 including an addressable heater thermally coupled to said reaction chamber.
- 67. (New) The low-volume hybridization device of claim 66 including a thermal insulation in contact with said heater.
- 68. (New) The low-volume hybridization device of claim 66 including a temperature sensor positioned adjacent said heater.
- 69. (New) The low-volume hybridization device of claim 45, including a cooler thermally coupled to said reaction chamber.
- 70. (New) The low-volume hybridization device of claim 69, wherein said cooler is a thermoelectric cooler.
- 71. (New) The low-volume hybridization device of claim 45 further including an extraction chamber constructed and arranged to exchange fluids with said reaction chamber.
- 72. (New) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.
- 73. (New) The low-volume hybridization device of claim 72, wherein said plug is a deformable plug.
- 74. (New) The low-volume hybridization device of claim 73, wherein said flexible diaphragm is constructed and arranged to compress said deformable plug for removing trapped liquids.

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75. (New) The low-volume hybridization device of claim 72, wherein said plug comprises glass wool.

- 76. (New) The low-volume hybridization device of claim 72, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.
- 77. (New) The low-volume hybridization device of claim 76, wherein said agent is selected from the group consisting of acids, bases, silanes, polysine, tethered antibodies, synthesized nucleic acids, and Poly-T DNA.
- 78. (New) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.
- 79. (New) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a structure comprising an open cell foam.
- 80. (New) The low-volume hybridization device of claim 71, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.
- 81. (New) The low-volume hybridization device of claim 80, wherein said affinity surface includes controlled-pore glass structures.
- 82. (New) The low-volume hybridization device of claim 80, wherein said affinity surface has glass spheres attached thereto.
- 83. (New) The low-volume hybridization device of claim 80, wherein said affinity surface has cellulose particles attached thereto.
- 84. (New) The low-volume hybridization device of claim 80, wherein said affinity surface is microfabricated.

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85. (New) The low-volume hybridization device of claim 80, wherein said affinity surface is machined.

- 86. (New) The low-volume hybridization device of claim 80, wherein said affinity surface is injection molded.
- 87. (New) The low-volume hybridization device of claim 45 further including a base-unit including a manifold constructed and arranged to control said flexible diaphragm.
- 88. (New) The low-volume hybridization device of claim 87 wherein said manifold is a vacuum manifold.
- 89. (New) The low-volume hybridization device of claim 87 wherein said baseunit further includes flow connectors for delivering fluid to said reaction chamber.
- 90. (New) The low-volume hybridization device of claim 87 wherein said baseunit further includes electrical connectors for controlling operation within said device.
  - 91. (New) A low-volume hybridization device, comprising: a base.
- a reaction chamber disposed in said base, said reaction chamber being bound by a flexible diaphragm,
  - a probe array disposed in said reaction chamber, and
- a processing chamber connectable to said reaction chamber and constructed for exchanging fluids with said reaction chamber.
- 92. (New) The low-volume hybridization device of claim 91 including a pneumatic manifold constructed and arranged to deflect said flexible diaphragm for exchange fluids between said reaction chamber and said processing chamber.

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93. (New) The low-volume hybridization device of claim 92 wherein said processing chamber includes an amplification chamber.

- 94. (New) The low-volume hybridization device of claim 93 wherein said amplification chamber is constructed for PCR amplification.
- 95. (New) The low-volume hybridization device of claim 92 wherein said processing chamber includes a sample acquisition chamber.
- 96. (New) The low-volume hybridization device of claim 92 wherein said processing chamber includes an extraction chamber.
- 97. (New) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.
- 98. (New) The low-volume hybridization device of claim 97, wherein said plug is a deformable plug.
- 99. (New) The low-volume hybridization device of claim 98, wherein said flexible diaphragm is constructed and arranged to compress said deformable plug for removing trapped liquids.
- 100. (New) The low-volume hybridization device of claim 97, wherein said plug comprises glass wool.
- 101. (New) The low-volume hybridization device of claim 97, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.

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- 102. (New) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.
- 103. (New) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a structure comprising an open cell foam.
- 104. (New) The low-volume hybridization device of claim 96, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.
- 105. (New) The low-volume hybridization device of claim 104, wherein said affinity surface includes controlled-pore glass structures.
- 106. (New) The low-volume hybridization device of claim 104, wherein said affinity surface has glass spheres attached thereto.
- 107. (New) The low-volume hybridization device of claim 104, wherein said affinity surface has cellulose particles attached thereto.
- 108. (New) The low-volume hybridization device of claim 104, wherein said affinity surface is microfabricated.
- 109. (New) The low-volume hybridization device of claim 104, wherein said affinity surface is machined.
- 110. (New) The low-volume hybridization device of claim 104, wherein said affinity surface is injection molded.